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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/618,143	07/11/2003	Paz Einat	2094/6773-A/JPW/FHB	8204

7590 09/07/2007

John P. White
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EXAMINER	
REDDIG, PETER J	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
09/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/618,143	EINAT ET AL.	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *3-5,8-10 and 12-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6,7,11 and 25-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/18/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

1. The Amendment filed June 18, 2007 in response to the Office Action of December 14, 2006 is acknowledged and has been entered. Claims 1, 2, 6, 7, 11, 25 and 26 have been amended and new claims 27 and 28 have been added.

2. Claims 1-28 are pending

3. Claims 3-5, 8-10, and 12-24 have been previously withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

4. Claims 1, 2, 6, 7, 11, and 25-28 as drawn to siRNA as the IDH inhibitor are currently under consideration.

5. The following rejections are being maintained:

Specification

6. The amendment filed 11/03/2006 remains objected to and the amendment filed June 18, 2007 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure, the new SEQ ID NO: 6 as set forth in section 5, page 3 of the Office Action of December 14,

Applicants argue that this error was an obvious typographical error. Support for the amendment can be found throughout the specification, siRNA molecules are known in the art as molecules composed of ribonucleotides, and not deoxyribonucleotides. The present specification states that siRNA refers to "an RNA molecule which decreases or silences the expression of a gene/ mRNA of its endogenous or cellular counterpart" (page 4, lines 17-19). Furthermore, the specification states: "[W]hen RNA sequences are said to be similar, or to have a degree of sequence identity or homology with DNA sequences, thymidine (T) in the DNA sequence is considered equal to uracil (U) in the RNA sequence. RNA sequences within the scope of the invention can be derived from DNA sequences or their complements, by substituting thymidine

(T) in the DNA sequence with uracil (U). RNA sequences within the scope of the invention can be derived from DNA sequences or their complements, by substituting thymidine (T) in the DNA sequence with uracil (U)" (page 29, lines 19-25).

Applicants argue that it is clear from the present application that the sequence identified as SEQ ID NO: 6 is an siRNA, and that an amendment changing the T nucleotides to U nucleotides is not new matter because (i) it is clear from the subject application that the sequence identified as SEQ ID NO: 6 is the sequence of an RNA, not DNA; (ii) RNA sequences do not contain T, but U instead; and (iii) the error was typographical in nature.

Applicants state that they have amended the specification to change the T nucleotides to U nucleotides in the sequence listed on page 39, line 15. Applicants note that this sequence is a siRNA sequence identified as SEQ ID NO: 6. Applicants maintain that this sequence erroneously contained T nucleotides instead of U nucleotides due to a typographical error. For the reasons stated in the paragraphs above, it is clear from the present application that applicants intended the sequence listed on page 39, line 15, to be an siRNA, and that an amendment changing the T nucleotides to U nucleotides does not constitute new matter.

Applicants' arguments have been carefully considered, but have not been found persuasive. Although the specification teaches that siRNA refers to "an RNA molecule which decreases or silences the expression of a gene/ mRNA of its endogenous or cellular counterpart." The specification also teaches that the present invention therefore comprises an siRNA molecule for the IDH gene, having the sequence set forth in Figure 4 (SEQ ID NO: 6), and a vector comprising said siRNA, see page 4, lines 26-28. Vectors commonly used for expression of siRNA are DNA based vectors such as Adenovirus which encode the siRNA on the DNA level

and then the siRNA is eventually expressed as RNA and the teachings of the specification do not limit the vector to RNA vectors only. Furthermore the specification teaches that an "Expression vector" refers to vectors that have the ability to incorporate and express heterologous DNA fragments in a foreign cell, see p. 8, lines 11-12. Thus, one of skill in the art would not necessarily recognize that SEQ ID NO: 6 should be an RNA sequence. Furthermore, both of the sequence listings filed refer to SEQ ID NO: 6 as a DNA molecule as the definition of the type of molecule SEQ ID NO: 6 is, see the numeric identifier <212> for SEQ ID NO: 6 in both sequence listings filed. Thus, the originally filed SEQ ID NO: 6 appears to have been intended to be a DNA molecule. Thus, Applicants arguments have not been found persuasive and the objection is maintained.

7. The disclosure remains objected to for the misspelling of polynucleotide as set forth in section 7, page 4, of the Office Action of December 14, 2006.

Applicants note that the word "polynucleotides" is correctly spelled in the heading on page 54 of the application as filed. Applicants note that the typographical error appears in the published document, i.e. U.S. Patent Application Publication No. 2004/0067234 A1. Specifically, in the heading preceding paragraph [0267] of the published document, the word "polynucleotides" is misspelled as "Polynucle Tides." Applicants maintain that the subject application as filed does not include this typographical error, and therefore no amendment is required.

Applicants' arguments have been carefully considered, but have not been found persuasive. The specification received by the Office on July 11, 2003 contains the misspelling on page 54 as previously set forth. The document can be viewed in Public Pair at

http://portal.uspto.gov/external/portal/pair. Thus, Applicants' arguments have not been found persuasive and the objection is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 2, 6, 7, 11, 25, and 26 remain rejected and new claims 27 and 28 are rejected for the reasons previously set forth in section 9, pages 4-11 of the Office Action of December 14, 2006.

Applicants argue that the disclosure of the subject specification and the knowledge in the art provide sufficient guidance for one skilled in the art to readily use the claimed invention. Specifically, applicants draw the Examiner's attention to the specification on page 21, line 16 to page 22, line 17, which discloses an *in vivo* application of the subject invention. In addition, by way of example, the specification discloses that *ex vivo* gene therapy requires the isolation and purification of patient cells, the introduction of a therapeutic gene, and the introduction of genetically altered cells into the patient. The specification also discloses several approaches to *in vivo* gene therapy such as "packaging" the therapeutic gene for administration to a patient in liposomes or in a replication-deficient virus, directly injecting the therapeutic gene into the bloodstream, or introducing the therapeutic gene into the target tissue by microparticle bombardment. The specification further discloses that gene therapy vectors can be delivered to a patient by, for example, intravenous injection, local administration, or stereotactic injection.

Applicants' arguments have been carefully considered, but have not been found persuasive. The generic disclosure of gene therapy techniques does not enable the claims, because, as previously set forth, the in vitro studies taught in the specification cannot be predictably extrapolated to *in vivo* responses because of the well known artifactual nature of cell culture and the unpredictability of drug development for apoptosis-related diseases such as cancer. Thus, without *in vivo* data in an appropriate model system demonstrating that siRNA to IDH can treat an apoptosis-related disease, one of skill in the art would not believe it more likely than not that one could predictably treat an apoptosis-related disease without undue experimentation.

Applicants argue that experimental data demonstrating the inhibition of IDH expression promoting cell death is provided *inter alia* in the subject specification. Several experimental systems were used to show the direct link between inhibition of IDH and apoptosis. Example IIC on pages 39-40 of the subject application discloses a gain of function assay which demonstrates that IDH expression protects cells from apoptosis. The results are depicted as the percentage of cells protected from apoptosis (Figure 9A) and the percentage of cell survival (Figure 9B), following anti-Fas induced apoptosis in cells ectopically expressing IDH. The inhibition assays further corroborate this result. In addition, the subject application discloses at page 14 examples of small molecules that are inhibitors of IDH. Example IV on pages 44-50 of the subject application discloses screening assays for identifying and isolating IDH inhibitors.

Applicants' arguments have been carefully considered, but have not been found persuasive because, as previously set forth and above, the in vitro studies taught in the specification cannot be predictably extrapolated to *in vivo* responses because of the well known

artifactual nature of cell culture and the unpredictability of drug development of apoptosis-related diseases such as cancer. Furthermore, applicants' arguments drawn to small molecule inhibitors and screening assays for identifying and isolating IDH inhibitors are not persuasive because Applicants are arguing limitations not found in the claims, as the claims are drawn to a method of treatment with an siRNA to IDH.

Applicants argue that they have submitted herewith documents that further substantiate the nexus between expression of IDH and tumorigenesis in various tissue types. Document number 1 (attached hereto as Exhibit I) establishes that the expression of fifteen proteins including IDH1 was up regulated in esophageal squamous cell carcinoma tissue compared to the expression in adjacent normal epithelium. Document number 2 (attached hereto as Exhibit 2) discloses that microarray analysis identified a 41-fold up-regulation of the expression of IDH1 in non-functional pituitary adenomas.

Applicants' arguments have been carefully considered, but have not been found persuasive because the evidence presented is not commensurate in scope with the claimed invention because the claims are drawn a method of treatment with an siRNA to IDH an neither submitted document teaches the treatment of any apoptosis related disease with an siRNA to IDH.

Applicants argue that with regard to no establishment of a nexus between the treatment of the cells with siRNA for the IDH gene and an effect on any IDH polypeptide, Applicants maintain that the specification discloses the nexus between the treatment of cells and the effect on the IDH polypeptides now claimed. Specifically, as disclosed in Example IIA on pages 38-39 and in Figures 7 and 8 of the subject application, antisense treatment created greater sensitivity to

FAS-mediated apoptosis and Doxorubicin-mediated apoptosis in HeLa cells which were stably transfected with a vector harboring an IDH1 specific antisense molecule (IRT-4Cl) than in "control" HeLa cells transfected with an empty vector. The subject application also discloses in Example IIB on page 39 that transiently transfecting HeLa cells with an IDH siRNA induced apoptosis in the HeLa cells when they were treated with doxorubicin.

Applicants point to the results presented in Example II (pages 38-40), in which ectopic expression of IDH results in protection of cells from apoptosis for enabling support. Applicants argue that, furthermore, inhibition of IDH with either an antisense or a siRNA molecule leads to increased sensitivity of cells to apoptosis. Applicants argue that the siRNA results are corroborated with antisense results, demonstrating siRNA specificity for the IDH gene.

Applicants' arguments have been carefully considered, but have not been found persuasive. Although the siRNA and antisense RNA to IDH induced greater sensitivity to apoptosis, the specification has not demonstrated that either the siRNA or antisense to IDH as any effect on the levels of IDH1 mRNA or protein in any system. Even if it were found that the siRNA to IDH specifically inhibit IDH mRNA or protein, one of skill in the art could not predictably use the siRNA for treatment because of the unpredictability of using small nucleic acid molecules for treatment as previously set forth.

Thus, Applicants' arguments have not been found persuasive and the objection is maintained.

8. Claims 1, 2, 6, 7, 11, 25, and 26 remain rejected and new claims 27 and 28 are rejected for the reasons previously set forth in section 10, pages 11-17 of the Office Action of December 14, 2006.

Applicants argue that amended claims 1, 7, 25 and 26 recite the IDH polypeptide as an IDH polypeptide having a sequence as set forth in SEQ ID NO: 2 or SEQ ID NO: 4 or having a sequence modified therefrom while retaining the biological properties of IDH. Applicants argue that the claimed modified IDH polypeptides do not include *any and every* homolog of the IDH polypeptide. Rather, the claimed modified IDH polypeptides must be related to the IDH polypeptides identified by SEQ ID NO: 2 or SEQ ID NO: 4 while retaining the biological properties of IDH. Applicants note that the Examiner's assertion that alterations of even a single amino acid in a polypeptide sequence can, in some cases, dramatically affect the biological activity and characteristics of the protein is therefore moot, because the claimed modified IDH polypeptides retain the biological activity of the IDH polypeptide.

Applicants' arguments have been carefully considered, but have not been found persuasive because the claims are now drawn to IDH polypeptides that retain the biological properties of IDH, but the specification does not teach what biological property of IDH a given polypeptide must retain to be usefully targeted for treating an apoptosis related disease and does not teach which amino acids are critical to that function. Furthermore, the polypeptides that retain the biological properties of IDH still read on variant IDH polypeptides which are not enabled because 1) there are no teachings that the variant polypeptides will function in the method claimed, i.e. as an IDH polypeptide that when inhibited will allow for treatment of an apoptosis-related disease and one could not predictably identify which molecules would act as inhibitors of these broadly claimed IDH polypeptides 2) the claims as broadly written are drawn to splice variants of IDH and one of ordinary skill in the art could not predictably identify which molecules would act as inhibitors of these broadly claimed IDH polypeptides 3) the single

siRNA for IDH taught in the specification would not be expected to inhibit the scope of IDH polypeptides contemplated because it is well known in the art that siRNAs are sequence specific inhibitors of mRNA and the single siRNA taught in the specification (SEQ ID NO: 6) would not be predicted to inhibit the numerous IDH mRNAs for the numerous variants of IDH polypeptide contemplated for the reasons previously set forth.

Thus, Applicants' arguments have not been found persuasive and the objection is maintained.

9. Claims 1, 2, 6, 7, 11, 25, and 26 remain rejected and new claims 27 and 28 are rejected for lacking an adequate written description for the reasons previously set forth in section 11, pages 17-21 of the Office Action of December 14, 2006.

Applicants argue that they have amended claims 1, 7, 25 and 26 to recite the IDH polypeptide having a sequence as set forth in SEQ ID NO: 2 or SEQ ID NO: 4 or having a sequence modified therefrom while retaining the biological properties of IDH. Applicants maintain that the specification adequately describes the claimed genus of IDH polypeptides (see *inter alia*, page 6, line 14 to page 7, line 5; page ii, lines 23-33; and Figures 1, 2, and 6). Applicants again maintain that the claimed modified IDH polypeptides do not include *any and every* homolog of the IDH polypeptide. Rather, the claimed modified IDH polypeptides are related to the IDH polypeptides identified by SEQ ID NO: 2 or SEQ ID NO: 4 while retaining the biological properties of IDH.

Applicants' arguments have been carefully considered, but have not been found persuasive because the claims are still drawn to a genus of variant IDH polypeptides that retain the biological properties of IDH, but the specification does not teach what biological property of

IDH a polypeptide must retain to be usefully targeted for treating an apoptosis related disease. Thus, as previously set forth, the specification does not describe the broadly claimed IDH polypeptides to be inhibited for treatment of an apoptosis related disease in a manner that satisfies either the Lilly or Enzo standards

Thus, Applicants' arguments have not been found persuasive and the objection is maintained.

10. Claims 25 and 26 remain rejected for lacking an adequate written description for the reasons previously set forth in section 12 pages 21-24 of the Office Action of December 14, 2006.

Applicants argue that they have amended claims 25 and 26 and added new claims 27 and 28 to recite the siRNA comprising nucleotides have a sequence as set forth in SEQ ID NO: 6. Applicants argue that the specification adequately describes the claimed genus of siRNA (see *inter alia,* page 4, lines 17-28; page 14, lines 26-28; page 15, line 19 to page 17, line 7; page 39, lines 12-21; and Figure 4). Applicants maintain that the claimed siRNAs do not include siRNAs specific to *any and every* homolog of the IDH polypeptide, but only those siRNAs specific to the IDH polypeptides of SEQ ID NO: 2 or SEQ ID NO: 4 or having a sequence modified therefrom while retaining the biological activity of the IDH polypeptide.

Applicants' arguments have been carefully considered, but have not been found persuasive because the claims are still drawn to a genus of variant IDH polypeptides that retain the biological properties of IDH and the specification does not describe the siRNAs for the genus of genes that encode the broadly claimed IDH polypeptides that retain the biological properties of IDH that satisfies either the Lilly or Enzo standards.

Thus, Applicants' arguments have not been found persuasive and the objection is maintained.

New Grounds of Rejection/Objection

Drawings

11. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: Figure 1A, 1B, 5A, and 5B. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

12. The sequence listing filed October 6, 2006, for improper identification of SEQ ID NO: 6 as a DNA molecule. Applicants are required to properly identify the type of molecule submitted in the sequence listing under the numeric identifier <212>, see 37 CFR 1.823(b) and MPEP 2424.02. Applicants have noted that SEQ ID NO: 6 is an RNA molecule, see above, thus the identification of the molecule as a DNA is improper. Applicants must provide a computer readable form (CRF) copy of the sequence listing, an initial or substitute paper copy of the

sequence listing, as well as any amendment directing its entry into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e-f) or 1.825(b) or 1.825(d). *Failure to supply the appropriate sequences identification numbers in response to this action will be considered non-responsive.*

Claim Rejections - 35 USC § 112

13. Claims 27 and 28 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation of SEQ ID NO: 6 claimed in Claims 27 and 28 has no clear support in the specification and the claims as originally filed for the reasons set forth above in section 6. The subject matter claimed in claims 27 and 28 broadens the scope of the invention as originally disclosed in the specification.

14. All other objections and rejections recited in Office Action of December 14, 2006 are withdrawn.

15. No claims allowed.

16. This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited either to an appeal to the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

If applicant should desire to appeal any rejection made by the examiner, a Notice of Appeal must be filed within the period for reply identifying the rejected claim or claims appealed. The Notice of Appeal must be accompanied by the required appeal fee.

If applicant should desire to file an amendment, entry of a proposed amendment after final rejection cannot be made as a matter of right unless it merely cancels claims or complies with a formal requirement made earlier. Amendments touching the merits of the application which otherwise might not be proper may be admitted upon a showing a good and sufficient reasons why they are necessary and why they were not presented earlier.

A reply under 37 CFR 1.113 to a final rejection must include the appeal form, or cancellation of, each rejected claim. The filing of an amendment after final rejection, whether or not it is entered, does not stop the running of the statutory period for reply to the final rejection unless the examiner holds the claims to be in condition for allowance. Accordingly, if a Notice of Appeal has not been filed properly within the period for reply, or any extension of this period obtained under either 37 CFR 1.136(a) or (b), the application will become abandoned.

17. Applicants' amendment necessitated the new grounds of rejection. Thus, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. ' 1.136(a).

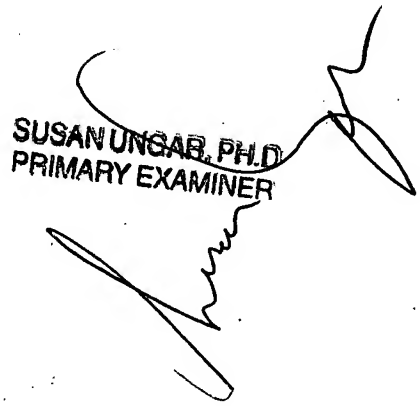
A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. ' 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0890. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Peter J. Reddig
Examiner
Art Unit 1642



PJR

Notice to Comply	Application No. 10/618,143	Applicant(s) Einat et al.	
	Examiner Peter J. Reddig	Art Unit 1642	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: The disclosure is lacking numerous sequence identifiers and sequence ID numbers, see the section titled "Sequence Listing" in the accompanying First Office Action on the Merits.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
For CRF Submission Help, call (703) 308-4212 or 308-2923
PatentIn Software Program Support
Technical Assistance.....703-287-0200
To Purchase PatentIn Software.....703-306-2600

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY

Sequence Count Sheet	Application/Control No.	Applicant(s)	
	10/618,143	Einat et al.	
	Examiner	Art Unit	
	Peter Reddig	1642	

DATE OF COUNT

Mark only one space below

☐ **(CRFN)** (CRF is unreadable; use CRF Diskette Problem Report)

☐ **(CRFD)** (CRF does not comply; use Notice to Comply)

☐ **(CRFR)** (CRF required but none submitted; use Notice to Comply)

☒ **(bona fide)** (second or subsequent letter to applicant reporting bona fide attempt to comply; use Notice to Comply and send copy of RSL)

☐ **(non bona fide)** (second or subsequent letter to applicant reporting non-bona fide attempt to comply; use Notice to Comply and send copy of RSL)

UNITED STATES PATENT AND TRADEMARK OFFICE

COMMISSIONER FOR PATENTS
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APPLICATION NO. /CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
10/618,143	07/11/2003	Paz Einat	2094/6773-A/JPW/FHB

EXAMINER	
Peter Reddig, Ph.D.	
ART UNIT	PAPER
1642	

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

The sequence listing filed October 6, 2006, for improper identification of SEQ ID NO: 6 as a DNA molecule. Applicants are required to properly identify the type of molecule submitted in the sequence listing under the numeric identifier <212>, see 37 CFR 1.823(b) and MPEP 2424.02.

If a complete reply has not been submitted by the time period set in the accompanying Office action (paper No 20061129) has expired, this application will become abandoned under 37 CFR 1.821(g).

Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for reply beyond the SIX MONTH statutory period. Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Please direct all replies to the United States Patent and Trademark Office via one (1) of the following:

1. Electronically submitted through EFS-Bio (http://ww.uspto.gov/ebc/efs/downloads/documents.htm>,

EFS Submission User Manual-ePAVE)

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3.Hand Carry, Federal Express, United Parcel Service or other delivery service to:

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter Reddig whose telephone number is 571-272-9031. The examiner can normally be reached on M-F 8:30 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached at 571-272-0890.

Peter Reddig, Ph.D.
Art Unit 1642

SUSAN UNGAR, PH.D
PRIMARY EXAMINER